

FIGURE 1

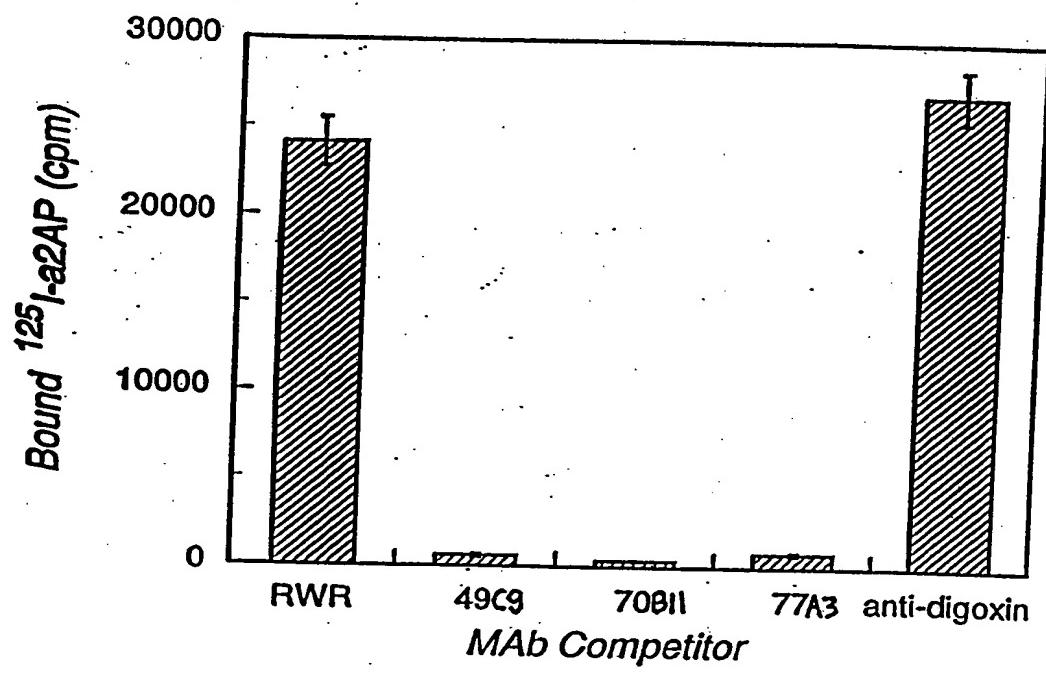


FIGURE 2

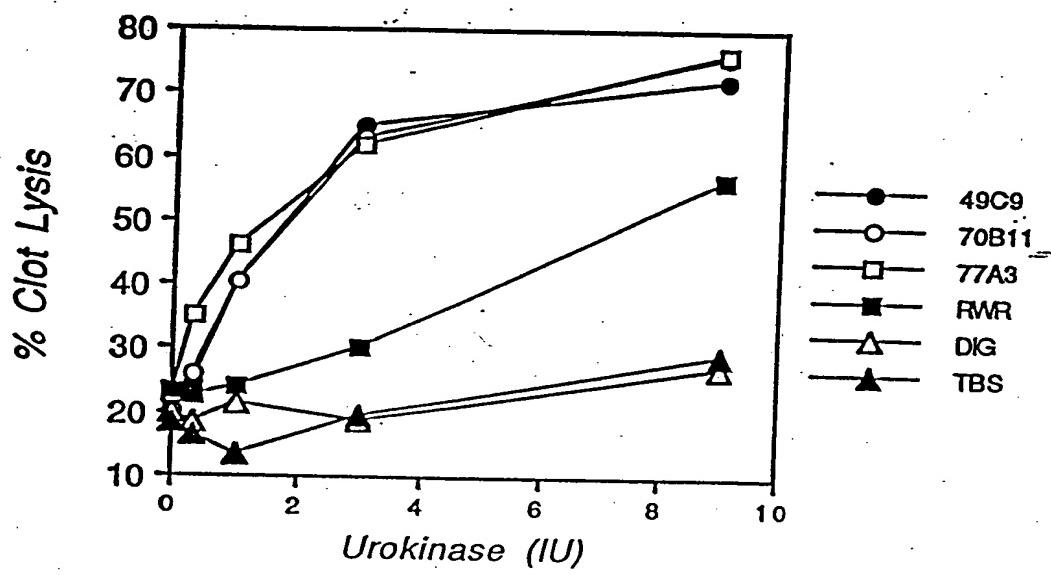


FIGURE 3

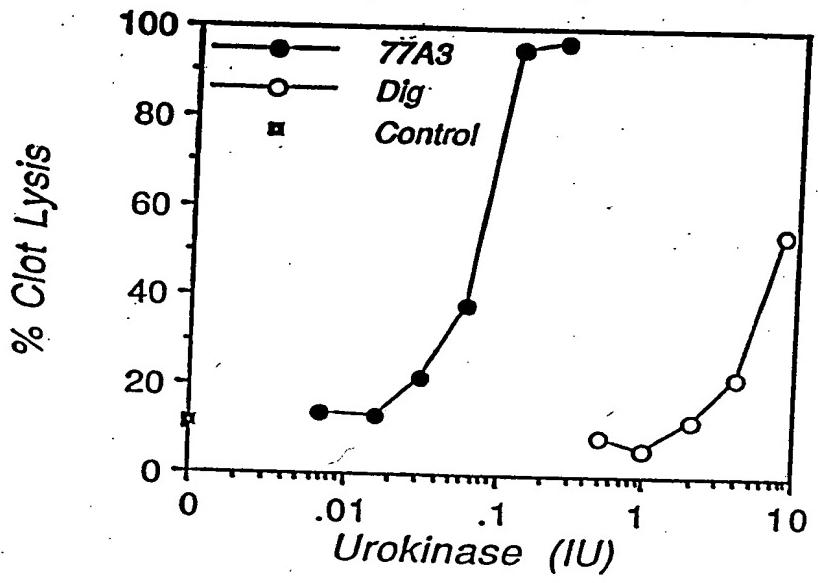
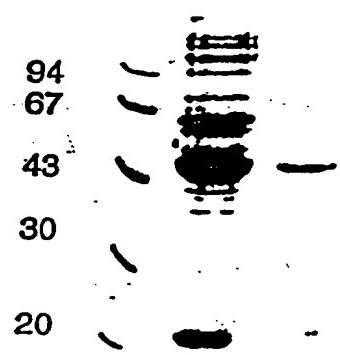


FIGURE 4



Std Ascites 77A3

FIGURE 5

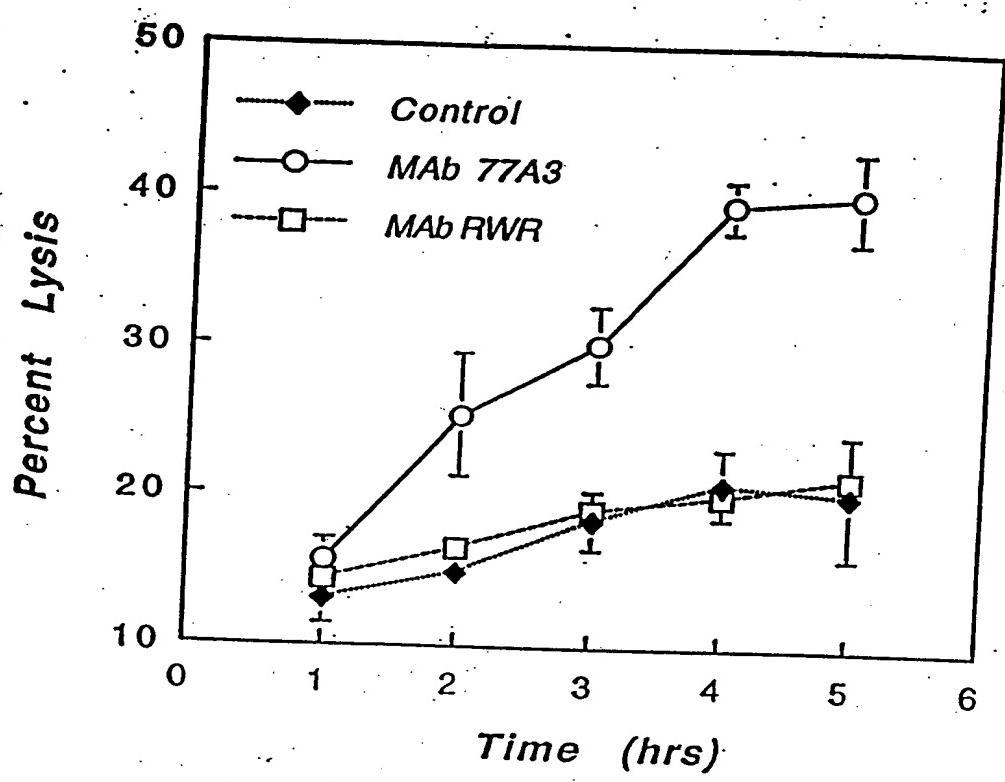


FIGURE 6

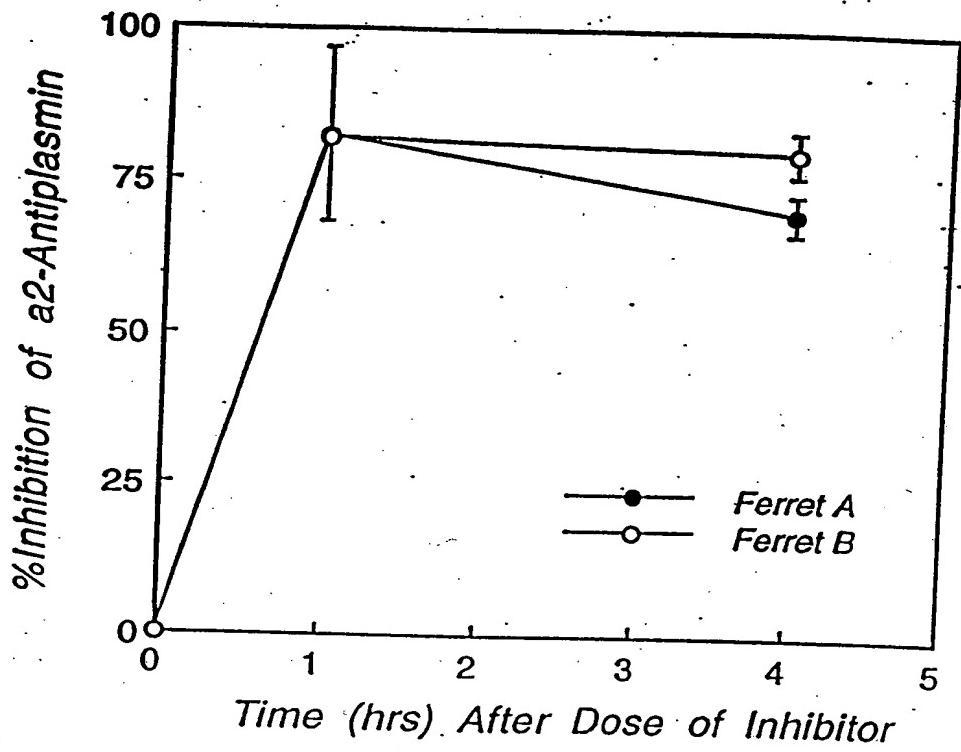


FIGURE 7

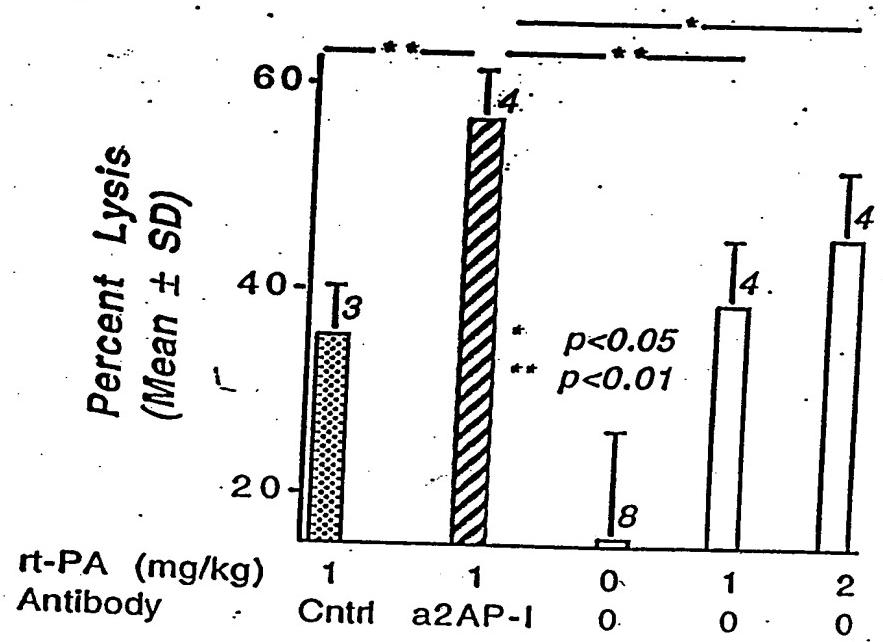


FIGURE 8

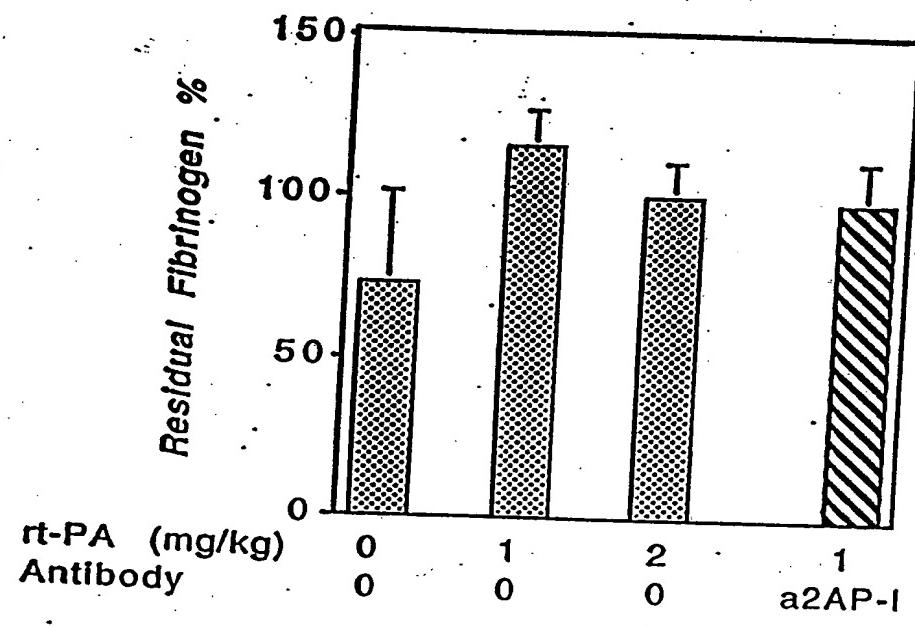


FIGURE 9

Fig. 10

MAb Light Chain	Amino Terminal Sequence
49C9	xIQMTQSPASLSASV
70B11	DIQMT
77A3	xIQMTQSPASLSASV

Fig. 11

10 20 30 40 50 60
* * G * * *
ATGAGTGTGC TCACTCAGGT CCTGGCGTTG CTGCTGCTGT GGCTTACAGG TGCCAGATGT
M S V L T Q V L G L L L L W L T G A R C>
A
70 80 90 100 110 120
* * * * * *
GACATCCAGA TGACTCAGTC TCCAGCCTCC CTATCTGCAT CTGTGGGAGA AACTGTCACC
D I Q M T Q S P A S L S A S V G E T V T>
130 140 150 160 170 180
* * * * * *
ATCACATGTC GAGCAAGTGG GAATATTCA AATTATTTAG CATGGTATCA GCAGAAACAG
I T C R A S G N I H N Y ' L A W Y Q Q K Q>
190 200 210 220 230 240
* * * * * *
GGAAAAATCTC CTCAGCTCCT GGTCTATAAT GCAAAAACCT TAGCAGATGG TGTGCCATCA
G K S P Q L L V Y N A K T L A D G V P S>
250 260 270 280 290 300
* * * * * *
AGGTTCACTG GCAGTGGATC AGGAACACAA TTTTCTCTCA GGATCAACAG CCTGCAGCCT
R F S G S G S G T Q F S L R I N S L Q P>
310 320 330 340 350 360
* * * * * *
GAAGATTTG GGAGTCATTA CTGTCAACAT TTTTGGACCA CTCCGTGGAC GTTCGGTGGAA
E D F G S H Y C Q H F W T T P W T F G G>
370 380
* *
GGCACCAAGC TGGAAATCAA A
G T K L E I K

Fig. 12

10 20 30 40 50 60
* * * * * *
ATGAGTGTGC TCACTCAGGT CCTGGGGTTG CTGCTGCTGT GGCTTACAGG TGCCAGATGT
M S V L T Q V L G L L L L W L T G A R C>

70 80 90 100 110 120
* * * * * *
GACATCCAGA TGACTCAGTC TCCAGCCTCC CTATCTGCAT CTGTGGGAGA AACTGTCACC
D I Q M T Q S P A S L S A S V G E T V T>

130 140 150 160 170 180
* * * * * *
GTCACATGTC GAGCAAGTGG GAATATTCAC AATTATTTAG CATGGTATCA GCAGAAACAG
V T C R A S G N I H N Y L A W Y Q Q K Q>

190 200 210 220 230 240
* * * * * *
GGAAAATCTC CTCAGCTCCT GGTCTATAAT GCAAGAACCT TAGCAGATGG TGTGCCATCA
G K S P Q L L V Y N A R T L A D G V P S>

250 260 270 280 290 300
* * * * * *
AGGTTCACTG GCAGTGGATC AGGAACACAA TATTCTCTCA AGATCAACAG CCTGCAGCCT
R F S G S G S G T Q Y S L K I N S L Q P>

310 320 330 340 350 360
* * * * * *
GAAGATTTTG GGAGTTATTA CTGTCAACAT TTTTGGAGTA ATCCGTGGAC GTTCGGTGGAA
E D F G S Y Y C Q H F W S N P W T F G G>

370 380
* *
GGCACCAAGC TGGAAATCAA
G T K L E I K

FIG. 13

10 20 30 40 50 60
* * * * * *
ATGAGTGTGC TCACTCAGGT CCTGGCGTTG CTGCTGCTGT GGCTTACAGG TGCCAGATGT
M S V L T Q V L A L L L L W L T G A R C>

70 80 90 100 110 120
* * * * * *
GACATCCAGA TGACTCAGTC TCCAGCCTCC CTATCTGCAT CTGTGGGAGA AACTGTCACC
D I Q M T Q S P A S L S A S V G E T V T>

130 140 150 160 170 180
* * * * * *
ATCACATGTC GAGCAAGTGG GAATATTACAC AATTATTTAG CATGGTATCA GCAGAAACAG
I T C R A S G N I H N Y L A W Y Q Q K Q>

190 200 210 220 230 240
* * * * * *
GGAAAATCTC CTCAAATCCT GGTCTATAAT GCAAAAACCT TAGCAGATGG TGTGCCATCA
G K S P Q L L V Y N A K T L A D G V P S>

250 260 270 280 290 300
* * * * * *
AGGTTCACTG GCAGTGGATC AGGAACACAA TTTTCTCTCA AGATCAACAG CCTGCAGCCT
R F S G S G S G T Q F S L K I N S L Q P>

310 320 330 340 350 360
* * * * * *
GAAGATTTG GGAGTCATTA CTGTCAACAT TTTTGGACCA CTCCGTGGAC GTTCGGTGG
E D F G S H Y C Q H F W T T P W T F G G>

370 380
* *
GGCACCAAGC TGGAAATCAA A
G T K L E I K

H2 HC (49c9 heavy chain) Fig. 14

9	19	29	39	49	59
*	*	*	*	*	*
ATGGMTTGG	GTGTGGAMCT	TGCTATTCCCT	GATGGCAGCT	GCCCAAAGTC	TCCAAGCACA
M A W	V W N	L L F L	M A A	A Q S	L Q A Q >
D T					
69	79	89	99	109	119
*	*	*	*	*	*
GATCCAGTTG	GTGCAGTCTG	GACCTGAGCT	GAAGAAGCCT	GGAGAAACAG	TCAAGATCTC
I Q L	V Q S	G P E	L K K P	G E T	V K I S >
129	139	149	159	169	179
*	*	*	*	*	*
CTGCAAGGCC	TCTGGGTATA	CCTTCACAAA	CTATGGAATG	AACTGGGTGA	AGCAGGGCTCC
C K A	S G Y	T F T N	Y G M	N W V	K Q A P >
189	199	209	219	229	239
*	*	*	*	*	*
AGGAAAGGGT	TTAAAGTGGA	TGGGCTGGAT	AAACACCAAG	AGTGGAGAGC	CAACATATGC
G K G	L K W	M G W I	N T K	S G E	P T Y A >
249	259	269	279	289	299
*	*	*	*	*	*
TGAAGAGTTC	AAGGGACGGT	TTGTCTTCTC	TTTGGAAACC	TCTGCCAGCA	CTGCCCATTT
E E F	K G R	F V F S	L E T	S A S	T A H L >
309	319	329	339	349	359
*	*	*	*	*	*
GCAGATCAAG	AATTCAGAA	ATGAGGACAC	GGCTACATAT	TTCTGTGCAA	GATGGGTACC
Q I K	N F R	N E D T	A T Y	F C A	R W V P >
369	379	389	399	409	
*	*	*	*	*	
TGGGACCTAT	GCTATGGACT	ACTGGGTCA	AGGAACCTCA	GTCACCGTCT	CCTCA
G T Y	A M D	Y W G Q	G T S	V T V	S S >

H3 HC (70B11 heavy chain) Fig. 15

10	20	30	40	50	60
*	*	*	*	*	*
ATGGMTTGGG	TGTGGAMCTT	GCTATTCCCTG	ATGGCAGCTG	CCCAAAGTAT	CCAAGCACAG
M A W	V W N L	L F L	M A A A	A Q S I	Q A Q >
D T					
70	80	90	100	110	120
*	*	*	*	*	*
ATCCAGTTGG	TGCAGTCTGG	ACCTGAGCTG	AAGAACGCTG	GAGAGACAGT	CAAGATCTCC
I Q L	V Q S G	P E L	K K P	G E T V	K I S >
130	140	150	160	170	180
*	*	*	*	*	*
TGCAAGGGCTT	CTGGGTATAAC	CTTCACAAAG	TATGGAATGA	ACTGGGTGAA	GCAGGCTCCA
C K A	S G Y T	F T K	Y G M	N W V K	Q A P >
190	200	210	220	230	240
*	*	*	*	*	*
GGAAAGGGTT	TAAAGTGGAT	GGGCTGGATA	AACACCAACA	GTGGAGAGCC	AACATATGCT
G K G	L K W M	G W I	N T N	S G E P	T Y A >
250	260	270	280	290	300
*	*	*	*	*	*
GAAGAGTTCA	AGGGACGGTT	TGCCTTCTCT	TTGGAAACCT	CTGCCAGCAC	TGCCTATTTG
E E F	K G R F	A F S	L E T	S A S T	A Y L >
310	320	330	340	350	360
*	*	*	*	*	*
CAGATCAACA	ACCTCAAAAAA	TGAGGACTCG	GCTACATATT	TCTGTGCAAG	ATGGGTACCT
Q I N	N L K N	E D S	A T Y	F C A R	W V P >
370	380	390	400	410	
*	*	*	*	*	
GGGACCTATG	CTATGGACTA	CTGGGGTCAA	GGAACCTCAG	TCACCGTCTC	CTCA
G T Y	A M D Y	W G Q	G T S	V T V S	S >

H4 HC (77A3 heavy chain) Fig. 16

10	20	30	40	50	60
*	*	*	*	*	*
ATGGMTTGGG TGTGGAMCTT GCTATTCTG ATGGCAGCTG CCCAAAGTAT CCAAGCACAG					
M A W	V W N L	L F L	M A A	A Q S I	Q A Q>
D T					
70	80	90	100	110	120
*	*	*	*	*	*
ATCCAGTTGG TGCAGTCTGG ACCTGAGCTG AAGAACGCTG GAGAACAGT CAAGATCTCC					
I Q L	V Q S G	P E L	K K P	G E T V	K I S>
130	140	150	160	170	180
*	*	*	*	*	*
TGCAAGGCTT CTGGGTATAC CTTCACAAAC TATGGAATGA ACTGGGTGAA GCAGGCTCCA					
C K A	S G Y T	F T N	Y G M	N W V K	Q A P>
190	200	210	220	230	240
*	*	*	*	*	*
GGAAAGGGTT TAAAGTGGAT GGGCTGGATA AACACCAAGA GTGGAGAGCC AACATATGCT					
G K G	L K W M	G W I	N T K	S G E P	T Y A>
250	260	270	280	290	300
*	*	*	*	*	*
GAAGAGTTCA AGGGACGGTT TGCCCTCTCT TTGGAAACCT CTGCCAGCAC TGCCAATTG					
E E F	K G R F	A F S	L E T	S A S T	A N L>
310	320	330	340	350	360
*	*	*	*	*	*
CAGATCAAGA ACCTCAAAAA TGAGGACACG GCTACATATT TCTGTGCAAG ATGGGTACCT					
Q I K	N L K N	E D T	A T Y	F C A R	W V P>
370	380	390	400	410	
*	*	*	*	*	
GGGACCTATG CCATGGACTA CTGGGGTCAA GGAACCTCAG TCACCGTCTC CTCA					
G T Y	A M D Y	W G Q	G T S	V T V S	S

h77A3-1 and h77A3-2 LIGHT CHAIN

۱۷۸۳

Humanized (aa)
Humanized at (sense)

Unpublished in (architects)

Signal Peptide

1 Loop

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15										
I	Q	M	T	Q	S	P	S	L	S	A	S	V	G	D	R	T	C	R	A	S	G	N	I	H	N
Y	L	A	W	E	X	A	Y	Z	B	C	D	F	G	H	I	J	K	L	M	N	O	P	Q	R	S

2 Loop

W Y Q Q K Q G K S P Q L L V Y N A K T L A S
6

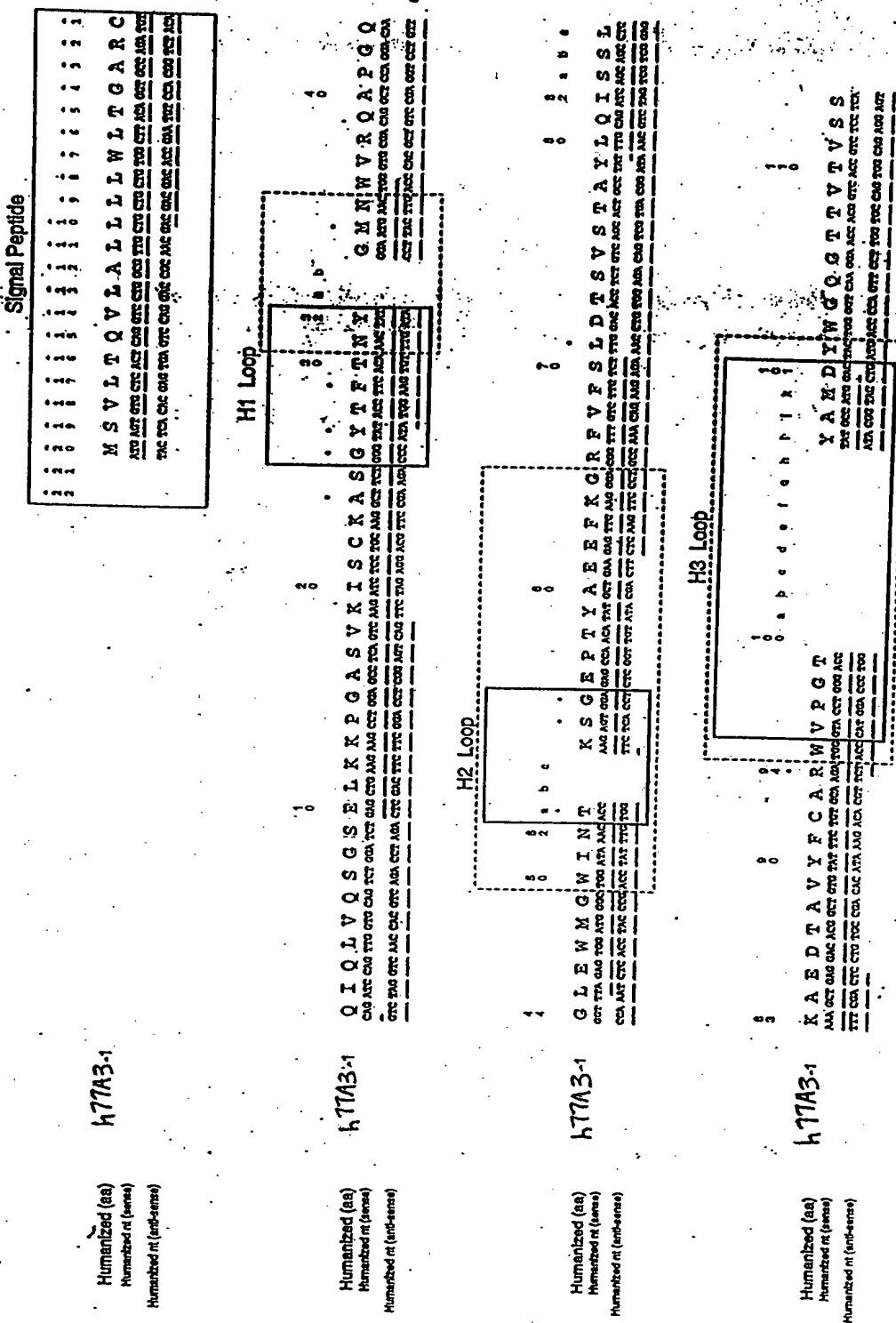
13400

Figure 17

h77A3-1 HEAVY CHAIN SEQUENCES

Humanized (ss)
Humanized (sense)
Humanized (antisense)

h77A3-1



h77A3-2 HEAVY CHAIN SEQUENCES

Figure 19

Humanized (aa)
Humanized et (ense)
Humanized et (ent-ense).

Signal Peptide

MSVLTQYLAELLWLTGARC
MSVLTQYLAELLWLTGARC
MSVLTQYLAELLWLTGARC
MSVLTQYLAELLWLTGARC

Humanized (as)
Humanized in (sense)
Humanized in (anti-sense)

Figure 20

Plasmin Assay
Murine, Chimeric and Humanized 77A3
6/3/97

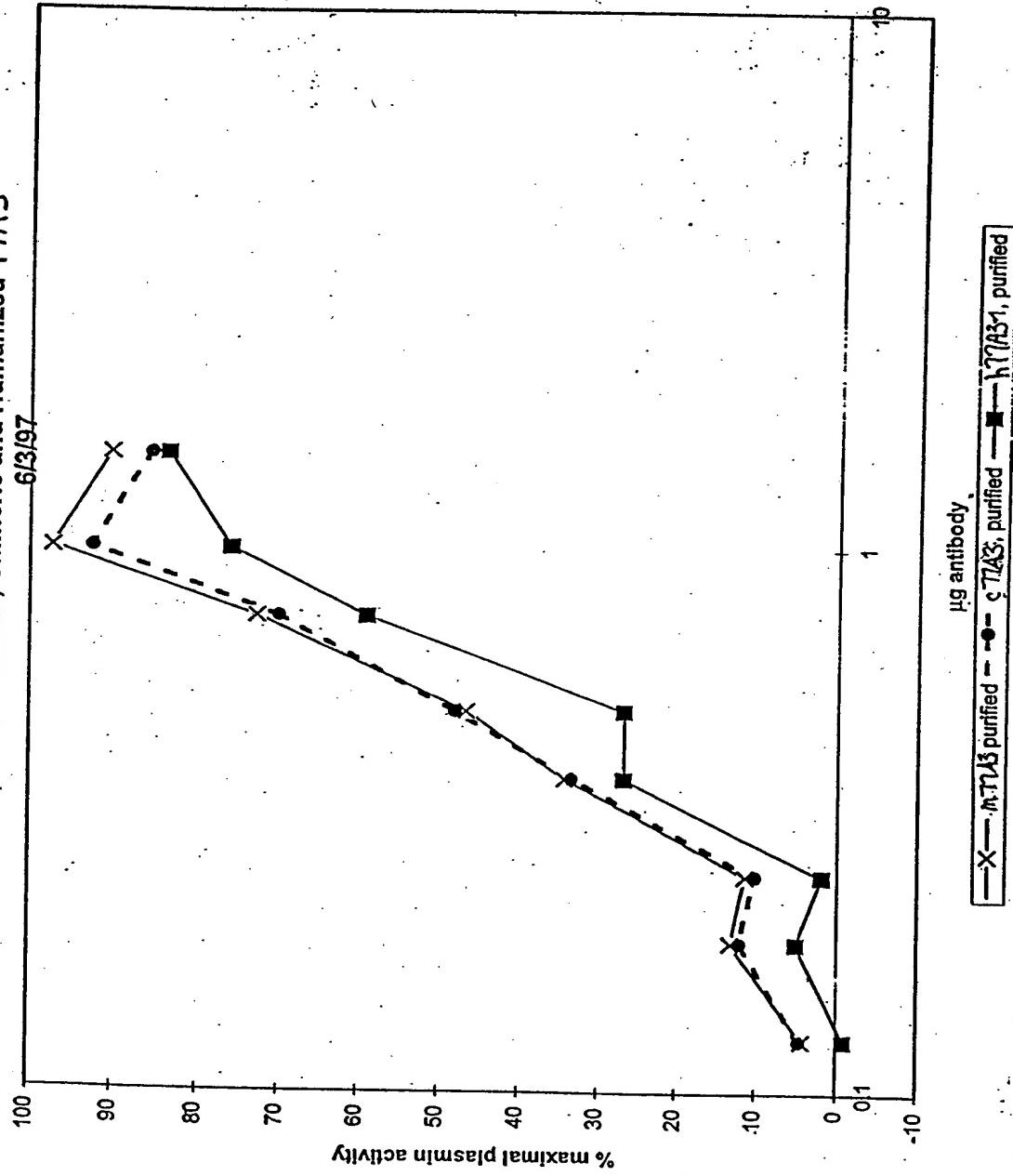


Figure 21

α_2 -antiplasmin antibody light chain sequences

	L1 Loop																																
h77A3-1 and h77A3-2	D	I	Q	M	T	Q	S	P	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	G	N	I	H	Y	L	A	
m77A3	D	I	Q	M	T	Q	S	P	A	S	L	S	A	S	V	G	E	T	V	T	I	T	C	R	A	S	G	N	I	H	Y	L	A
m49C9	D	I	Q	M	T	Q	S	P	A	S	L	S	A	S	V	G	E	T	V	T	I	T	C	R	A	S	G	N	I	H	Y	L	A
m70B11	D	I	Q	M	T	Q	S	P	A	S	L	S	A	S	V	G	E	T	V	T	V	T	C	R	A	S	G	N	I	H	Y	L	A
murine consensus	D	I	Q	M	T	Q	S	P	A	S	L	S	A	S	V	G	E	T	V	T	X	T	C	R	A	S	G	N	I	H	Y	L	A
77A3/49C9 consensus	D	I	Q	M	T	Q	S	P	A	S	L	S	A	S	V	G	E	T	V	T	I	T	C	R	A	S	G	N	I	H	Y	L	A
all	D	I	Q	M	T	Q	S	P	X	S	L	S	A	S	V	G	X	X	V	T	X	T	C	R	A	S	G	N	I	H	Y	L	A

	L2 Loop																																				
h77A3-1 and h77A3-2	W	Y	Q	Q	K	Q	G	K	S	P	Q	L	L	V	Y	N	A	K	T	L	A	S	G	V	P	S	R	F	S	G	S	G	T	D	F	T	L
m77A3	W	Y	Q	Q	K	Q	G	K	S	P	Q	L	L	V	Y	N	A	K	T	L	A	D	G	V	P	S	R	F	S	G	S	G	T	Q	F	S	L
m49C9	W	Y	Q	Q	K	Q	G	K	S	P	Q	L	L	V	Y	N	A	K	T	L	A	D	G	V	P	S	R	F	S	G	S	G	T	Q	F	S	L
m70B11	W	Y	Q	Q	K	Q	G	K	S	P	Q	L	L	V	Y	N	A	K	T	L	A	D	G	V	P	S	R	F	S	G	S	G	T	Q	Y	S	L
murine consensus	W	Y	Q	Q	K	Q	G	K	S	P	Q	L	L	V	Y	N	A	X	T	L	A	D	G	V	P	S	R	F	S	G	S	G	T	Q	X	S	L
77A3/49C9 consensus	W	Y	Q	Q	K	Q	G	K	S	P	Q	L	L	V	Y	N	A	X	T	L	A	D	G	V	P	S	R	F	S	G	S	G	T	Q	X	S	L
all	W	Y	Q	Q	K	Q	G	K	S	P	Q	L	L	V	Y	N	A	X	T	L	A	X	G	V	P	S	R	F	S	G	S	G	T	X	X	L	

	L3 Loop																																	
h77A3-1 and h77A3-2	I	S	S	L	Q	P	E	D	F	G	S	H	Y	C	Q	H	F	W	T	T	P	W	T	F	G	Q	Q	G	T	K	L	E	I	K
m77A3	I	N	S	L	Q	P	E	D	F	G	S	H	Y	C	Q	H	F	W	T	T	P	W	T	F	G	Q	Q	G	T	K	L	E	I	K
m49C9	I	N	S	L	Q	P	E	D	F	G	S	H	Y	C	Q	H	F	W	T	T	P	W	T	F	G	Q	Q	G	T	K	L	E	I	K
m70B11	I	N	S	L	Q	P	E	D	F	G	S	H	Y	C	Q	H	F	W	S	N	P	W	T	F	G	Q	Q	G	T	K	L	E	I	K
murine consensus	I	N	S	L	Q	P	E	D	F	G	S	X	Y	C	Q	H	F	W	X	X	P	W	T	F	G	Q	Q	G	T	K	L	E	I	K
77A3/49C9 consensus	I	N	S	L	Q	P	E	D	F	G	S	H	Y	C	Q	H	F	W	T	T	P	W	T	F	G	Q	Q	G	T	K	L	E	I	K
all	I	X	S	L	Q	P	E	D	F	G	S	X	Y	C	Q	H	F	W	X	X	P	W	T	F	G	Q	Q	G	T	K	L	E	I	K

Figure 22

α_2 -antiplasmin antibody heavy chain sequences

	H1 Loop				
h77A3-1	Q I Q L V Q S G S E L K K P G A S V K I S C K A S G Y T F T N Y				G M N W V R Q A P G Q
h77A3-2	Q I Q L V Q S G A E V K K P G A S V K I S C K A S G Y T F T N Y				G M N W V R Q A P G Q
m77A3	Q I Q L V Q S G P E L K K P G E T V K I S C K A S G Y T F T N Y				G M N W V K Q A P G K
m49C9	Q I Q L V Q S G P E L K K P G E T V K I S C X A S G Y T F T N Y				G M N W V K Q A P G K
m70B11	Q I Q L V Q S G P E L K K P G E T V K I S C X A S G Y T F T K Y				G M N W V K Q A P G K
humanized consensus	Q I Q L V Q S G X E X K K P G A S V K I S C K A S G Y T F T N Y				G M N W V R Q A P G Q
murine consensus	Q I Q L V Q S G P E L K K P G E T V K I S C X A S G Y T F T X Y				G M N W V K Q A P G K
77A3/49C9 consensus	Q I Q L V Q S G P E L K K P G E T V K I S C X A S G Y T F T N Y				G M N W V K Q A P G K
all	Q I Q L V Q S G X E X K K P G X X V K I S C X A S G Y T F T X Y				G M N W V X Q A P G X
	H2 Loop				
h77A3-1	G L E W M G W I N T	K S G E P T Y A E E F K G R P V F S L D T S V S T A Y L Q I S S L			
h77A3-2	G L E W M G W I N T	K S G E P T Y A E E F K G R F T F L L D T S T S T A Y L E I R S L			
m77A3	G L K W M G W I N T	K S G E P T Y A E E F K G R F A F S L E T S A S T A N L Q I K N L			
m49C9	G L K W M G W I N T	K S G E P T Y A E E F K G R F V F S L E T S A S T A H L Q I K N F			
m70B11	G L K W M G W I N T	N S G E P T Y A E E F K G R F A F S L E T S A S T A Y L Q I N N L			
humanized consensus	G L E W M G W I N T	K S G E P T Y A E E F K G R F X F X L D T S X S T A Y L X I X S L			
murine consensus	G L K W M G W I N T	X S G E P T Y A E E F K G R F X F S L E T S A S T A X L Q I X N X			
77A3/49C9 consensus	G L K W M G W I N T	K S G E P T Y A E E F K G R F X F S L E T S A S T A X L Q I K N X			
all	G L X W M G W I N T	X S G E P T Y A E E F K G R F X F X L X T S X S T A X L X I X X X			
	H3 Loop				
h77A3-1	K A E D T A V Y F C A R W V P G T				Y A M D Y W G Q Q G T T V T V S S
h77A3-2	R S D D T A V Y F C A R W V P G T				Y A M D Y W G Q Q G T T V T V S S
m77A3	K N E D T A T Y F C A R W V P G T				Y A M D Y W G Q Q G T S V T V S S
m49C9	R N E D T A T Y F C A R W V P G T				Y A M D Y W G Q Q G T S V T V S S
m70B11	K N E D S A T Y F C A R W V P G T				Y A M D Y W G Q Q G T S V T V S S
humanized consensus	X X X D T A V Y F C A R W V P G T				Y A M D Y W G Q Q G T T V T V S S
murine consensus	X N E D X A T Y F C A R W V P G T				Y A M D Y W G Q Q G T S V T V S S
77A3/49C9 consensus	X N E D T A T Y F C A R W V P G T				Y A M D Y W G Q Q G T S V T V S S
all	X X X D X A X Y F C A R W V P G T				Y A M D Y W G Q Q G T X V T V S S